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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,085	05/03/2006	Shinji Okano	50026/058001	5137

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
06/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,085	OKANO ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :3/6/08;1/9/08;10/15/07;7/23/07;7/16/07;3/14/07.

DETAILED ACTION

Claims 1-14 are pending in the present application, and they are examined on the merits herein.

Information Disclosure Statement

Certain documents such as search reports and preliminary examination report in cited IDS were lined through because they are not proper references. However, these documents were dated and signed because they were considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-12 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to a vector-comprising cell produced by the method of any one of claims 1 to 10. Since an embodiment of the instant claims encompasses a vector-comprising cell, including a vector comprising mature dendritic cell, produced by an *in vivo* method and wherein the cell is a human cell (see at least claim 10), such **a vector-comprising cell is integrated or present in a human being and therefore being an inseparable part of the human itself**. The scope of the claims, therefore, encompasses at least a part of a human being, which is a non-statutory subject matter.

The examiner notes that the insertion of the term "An isolated" in front of the term "vector-comprising cell" would obviate the above rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Steinman et al. (US 6,300,090).

Steinman et al disclose methods and compositions useful for delivering antigens (e.g., tumor antigens, viral antigens, bacterial antigens, autoimmune antigens) to dendritic cells which are then useful for inducing T antigen specific cytotoxic T lymphocytes in both *in vitro* and *in vivo*, wherein antigens are provided to dendritic cells using a viral vector such as vesicular stomatitis virus and influenza virus which may be modified to express non-native antigens for presentation to the dendritic cells (see at least Summary of the Invention). Steinman et al also teach that human dendritic cells can be obtained as mature dendritic cells from an appropriate tissue such as blood or bone marrow or by methods known in the art or as proliferating cultures of dendritic cell precursors, and the proliferating or mature dendritic cells are infected with the recombinant viral vectors delivering antigens (col. 7, line 61 continues to line 46 of col. 8); Col. 9, line 22 continues to line 49 of col. 10). Steinman et al further teach that the

dendritic cells expressing selected antigens can be administered into a mammal in need thereof at least via intravenous, intraperitoneal or intralesional route of delivery (col. 10, line 62 continues to line 39 of col. 11).

Accordingly, the teachings of Steinman et al meet all the limitation of the instant claims. Therefore, the reference anticipates the instant claims.

Claims 1-3, 6-8 and 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Song et al. (US 2002/0123479 A1).

Song et al disclose compositions and methods useful for stimulating an immune response against one or more disease associated antigens, including cancer associated antigens, by genetically modifying dendritic cells including dendritic progenitor cells, *in vivo* or *ex vivo*, wherein the dendritic cells were genetically modified by a recombinant negative strand RNA virus (e.g., vesicular stomatitis virus, paramyxoviruses, orthomyxoviruse and bunyaviruses) directing the expression of at least one disease associated antigen (see at least Summary of the Invention; particularly paragraphs 6-7, 10-12, 16-18, 41 and 60). Song et al also disclose that it has been disclovered that the efficiency of immune system stimulation mediated by genetically modifying dendritic cells can be several orders of magnifutde greater than that mediated by genetically modified fibroblasts, muscle, and other cell types (paragraph 39). Song et al further disclose that an expression vector may in addition to directing expression of at least one disease associated antigen, directs the expression of an immunomodulatory factor such as IL-12, IL15, IL-2, beta-interferon among many others (paragraphs 68, 89-90). Song

et al also teach that the genetically modifying dendritic cells are typically administered via parenteral or other traditional direct routes or directly into a specific tissue such as into the tumor in the case of cancer therapy in a mammal in need thereof (paragraphs 16-18 and 140).

Accordingly, the teachings of Song et al meet all the limitation of the instant claims. Therefore, the reference anticipates the instant claims.

Claims 1-2, 4 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Jin et al. (Gene therapy 10:272-277, February 2003; IDS) as evidenced by Romani et al. (J. Exp. Med. 180:83-93, 1994).

Jin et al disclose a method in which recombinant Sendai virus is in contact and provides a highly efficient gene transfer into human cord blood CD34+ cells, including human cord blood HSCs and more immature cord blood progenitor cells (see at least the abstract; page 276, col. 1, last paragraph). Human cord blood CD34+ cells comprises at least CD34+ precursor cells of dendritic cells as evidenced at least by the teachings of Romaini et al which disclose that CD34+ cord blood cells could give rise to dendritic cells under an appropriate culture conditions. It is further noted that the method of Jin et al has the same single method step and the same starting materials as the method being claimed.

Therefore, the teachings of Jin et al meet all the limitation of the claims as broadly written. Therefore, the reference anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (US 2002/0123479 A1) in view of Tokusumi et al. (US 6,746,860; IDS).

Song et al disclose compositions and methods useful for stimulating an immune response against one or more disease associated antigens, including cancer associated antigens, by genetically modifying dendritic cells including dendritic progenitor cells, *in vivo* or *ex vivo*, wherein the dendritic cells were genetically modified by a recombinant negative strand RNA virus (e.g., vesicular stomatitis virus, paramyxoviruses, orthomyxoviruse and bunyaviruses) directing the expression of at least one disease associated antigen (see at least Summary of the Invention; particularly paragraphs 6-7,

10-12, 16-18, 41 and 60). Song et al also disclose that it has been disclovered that the efficiency of immune system stimulation mediated by genetically modifying dendritic cells can be several orders of magnifutde greater than that mediated by genetically modified fibroblasts, muscle, and other cell types (paragraph 39). Song et al further disclose that an expression vector may in addition to directing expression of at least one disease associated antigen, directs the expression of an immunomodulatory factor such as IL-12, IL15, IL-2, beta-interferon among many others (paragraphs 68, 89-90). Song et al also teach that the genetically modifying dendritic cells are typically administered via parenteral or other traditional direct routes or directly into a specific tissue such as into the tumor in the case of cancer therapy in a mammal in need thereof (paragraphs 16-18 and 140).

Song et al did not teach explicitly the use of a Sendai virus vector for genetically modifying dendritic cells, even though they disclose that the dendritic cells could be genetically modified by any recombinant negative strand RNA virus including any paramyxovirus.

However, at the effective filing date of the present application, Tokusumi et al already disclosed the preparation of at least a recombinant Sendai virus vector to be used for transfer of foreign genes (see at least the abstract as well as Summary of the Invention). Tokusumi et al further disclosed that the Sendai virus vector is useful for gene therapy due to its safety, high gene transfer efficiency and capacity to express a foreign gene in a high level.

Accordingly, it would have been obvious and within the scope of skill for an ordinary skilled artisan to modify the teachings of Song et al. by also utilizing the recombinant Sendai virus vector taught by Tokusumi to genetically modifying the dendritic cells for expressing at least a disease associated antigen.

An ordinary skilled artisan would have been motivated to carry out the above modification because Tokusumi et al already taught that the recombinant Sendai virus vector is useful for gene therapy due to its safety, high gene transfer efficiency and capacity to express a foreign gene in a high level.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Song et al., Tokusumi et al., coupled with a high level of skill for an ordinary skilled artisan in the relevant art.

Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinman et al. (US 6,300,090) in view of Romani et al. (J. Exp. Med. 180:83-93, 1994).

Steinman et al disclose methods and compositions useful for delivering antigens (e.g., tumor antigens, viral antigens, bacterial antigens, autoimmune antigens) to dendritic cells which are then useful for inducing T antigen specific cytotoxic T lymphocytes in both *in vitro* and *in vivo*, wherein antigens are provided to dendritic cells using a viral vector such as vesicular stomatitis virus and influenza virus which may be modified to express non-native antigens for presentation to the dendritic cells (see at

least Summary of the Invention). Steinman et al also teach that human dendritic cells can be obtained as mature dendritic cells from an appropriate tissue such as blood or bone marrow or by methods known in the art or as proliferating cultures of dendritic cell precursors, and the proliferating or mature dendritic cells are infected with the recombinant viral vectors delivering antigens (col. 7, line 61 continues to line 46 of col. 8); Col. 9, line 22 continues to line 49 of col. 10). Steinman et al further teach that the dendritic cells expressing selected antigens can be administered into a mammal in need thereof at least via intravenous, intraperitoneal or intralesional route of delivery (col. 10, line 62 continues to line 39 of col. 11).

Steinman et al do not teach specifically a method for producing a gene transferred dendritic cell further comprising the step of culturing the cell in the presence of GM-CSF and IL-4 before or after contacting a minus-strand RNA viral vector with a dendritic cell or a precursor cell thereof.

However, at the effective filing date of the present application, Romaini et al already disclosed at least a method for generating proliferating human dendritic cells derived from CD34+ mononuclear cells obtained from normal human adult blood in a culture containing GM-CSF and IL-4 over a 5-7 day period (see at least the abstract; page 87, col. 2, last paragraph continues to col. 2, first paragraph of page 89). Romani et al further disclosed IL-4 was used to suppress monocyte development and the addition of GM-CSF led to the formation of large proliferating DC aggregates.

Accordingly, it would have been obvious and within the scope of skill for an ordinary skilled artisan to modify the teachings of Steinman et al. by at least culturing

CD34+ mononuclear cells obtained from normal human adult blood under the conditions in the presence of GM-CSF and IL-4 as taught by Romani et al for the preparation of dendritic cells prior to contacting the generated dendritic cells with a recombinant viral vector such as vesicular stomatitis virus and influenza virus.

An ordinary skilled artisan would have been motivated to carry out the above modification because Romaini et al already established such a condition for the preparation of large proliferating DC aggregates. Moreover, please also note that Steinman et al taught clearly that human dendritic cells can be obtained by any method known in the art.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Steinman et al., Romani et al. coupled with a high level of skill for an ordinary skilled artisan in the relevant art.

Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 6-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-8 of copending Application No. 11/630,532.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The instant claims are directed to a method for producing a gene transferred dendritic cell, which comprises the step of contacting a minus-strand RNA viral vector with a dendritic cell or a precursor cell thereof; a vector-comprising cell produced by the same method and a method for suppressing tumor growth comprising the step of delivering the same dendritic cells to a tumor cell.

Claims 1 and 4-8 of copending Application No. 11/630,532 are drawn to an anticancer agent comprising a dendritic cell introduced with an RNA virus able to replicate its genome, including the RNA virus encodes an IFN-beta; a method for producing the same anticancer agent and a method for suppressing a cancer comprising the step of administering a dendritic cell introduced with an RNA virus able to replicate its genome.

The claims of the present application differ from the claims of the copending Application No. 11/630,532 in reciting specifically minus-strand RNA viral vector, paramyxovirus vector or Sendai virus vector.

The claims of the present application can not be considered to be patentably distinct over claims 1 and 4-8 of copending Application No. 11/630,532 when there are specific disclosed embodiments of the copending Application that teach that the preferred RNA viruses of the invention include paramyxoviridae virus such as Sendai virus (page 5, lines 1-36; and examples); and dendritic cells include both mature and immature dendritic cells (page 8, lines 3-4). Accordingly, the claims of copending Application No. 11/630,532 fall within the scope of claims 1-3 and 6-13 of the present application.

This is because it would have been obvious to an ordinary skilled artisan to modify the claims of the copending Application by introducing a minus-strand RNA viral vector such as Sendai viral vector into dendritic cells (both mature and/or immature dendritic cells) for the preparation of an anticancer agent, that support the instant claims. An ordinary skilled artisan would have been motivated to do this because these embodiments are explicitly disclosed or taught in the copending Application No. 11/630,532 as preferred embodiments.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN, Ph.D./
Primary Examiner, Art Unit 1633